

# EXHIBIT G

## *Lindane Information* FACT CHECKER

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Groups seeking to ban the medical use of lindane have done a disservice to the public by spreading misleading information, often presented out of context, in the news media, on the Internet, and elsewhere about the risks and benefits of lindane. Repeatedly, their petitions to ban lindane medications have been rejected and determined to be without merit by scientific and medical experts working with the Food and Drug Administration (FDA) and the Environmental Protection Agency (EPA).

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## Setting The Record Straight About Lindane Medications

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- [Does lindane have more risks than benefits?](#)
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- [Does a single treatment of lindane pollute 6 million gallons of water?](#)
- [Is lindane the 32nd most toxic chemical in the environment?](#)
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### Misleading Claim:

Newer treatments for scabies and lice make lindane lotion and shampoo unnecessary and obsolete.

### Facts:

Although several treatment options are available for the management of scabies and lice, none are 100% effective. Furthermore, some patients are unable to tolerate certain medications because of allergies or adverse side effects. (See [The Need for Second-Line Medications like Lindane](#))

In many areas, drug-resistant forms of scabies and lice are on the rise, which further compromises the effectiveness of available medications and necessitates the need for a range of therapeutic options.<sup>1-6</sup> (See [Lindane and Resistance](#))

### Misleading Claim:

Manual removal of lice and nits with special combs or other mechanical means is the best treatment for infestation and prevention of recurrence.\*

## Facts:

The Centers for Disease Control and Prevention (CDC) and The American Academy of Pediatrics (AAP) designate pediculicidal medications as the preferred approach over manual removal for the treatment of head lice.<sup>7,8</sup> (See [Scabies and Lice Treatment Options](#))

In a rigorous head-to-head clinical study reported in the medical journal *Lancet*, manual removal of head lice with a commercial wet-combing kit was found to be less than half as effective as treatment with a prescription pediculicide.<sup>9</sup>

Moreover, use of combs is not relevant for the treatment of scabies—a widespread parasitic infection that requires a scabicial medication, such as lindane.

\* This claim is often made by the National Pediculosis Association (NPA), which holds itself out as a nonprofit health organization but actually makes its money by marketing a competitive medical device to lindane shampoo without employing a single licensed healthcare professional.

## Misleading Claim:

Lindane medications are no longer effective, with recently reported cure rates as low as 17%.

## Facts:

There are numerous relatively large clinical studies in patients that document high rates of cure for lindane medications similar to other commonly used medications for scabies and lice.<sup>2,10-13</sup>

In contrast, the above statement is based on research published by Meinking TL, et al. in 2002\* - the limitations of which are numerous. First, this study was an in vitro (i.e., test tube) analysis, meaning “cure rates” in patients were not even assessed. Further, the lack of sensitivity of “test tube” studies in predicting rates of effectiveness that would otherwise be noted in patients in a real-world use situation has been addressed by other scientific experts.<sup>5,14</sup> In fact, the recent 2006 Cochrane Systemic Review of head lice treatments (an independent, authoritative analysis of evidence-based research) excluded such studies for this very reason.<sup>14</sup>

Second, the study analyzed lice “samples” that were taken from approximately 25 patients in South Florida, where resistance to lindane had been previously reported.<sup>15</sup>

Thus, extrapolation of these findings to the rest of the nation has no scientific basis given that drug resistance and efficacy varies geographically, meaning state to state, city to city and setting to setting. (See [Lindane and Resistance](#))

\*Note that this small study was funded by the then manufacturer of Ovide® (malathion) - a competitive brand of head lice medication to lindane shampoo.

## Misleading Claim:

1 in 5 patients using lindane medications will experience a serious adverse event.

## Facts:

The above statement is false. The FDA has quantified serious adverse events (AEs) as rare when lindane medications are used properly<sup>16,17</sup> — an assessment that is based on

more than 50 years of prescription use in tens of millions of patients. The fact is that lindane medications are generally safe and well tolerated. The most common side effects are nonserious reactions of the skin, such as itching and dryness.<sup>18,19</sup> From 1951 to 2002, relatively few lindane-associated AEs were reported to the FDA through their Adverse Event Reporting System (AERS) database — just 488 total. The vast majority (85%) of these reports were nonserious, while serious events almost always resulted from product misuse. In fact, just 14 serious case reports arose from some cause other than misuse, which is considered “rare” and noted as such in the FDA-approved prescription labeling for both lindane lotion and lindane shampoo.<sup>6,17,18,19</sup> (Note that in 2003, lindane medications were limited to small, single-use bottles to mitigate the risk for misuse)

In striking contrast, acetaminophen (e.g., the active ingredient in Tylenol®) has been reported to cause roughly 500 deaths and over 50,000 emergency room admissions every year, yet it remains available without prescription.<sup>22</sup> The bottom line is that ALL medications are associated with side effects, even with proper use. First-line scabies and lice medications, including permethrin, malathion, crotamiton, and ivermectin, are no exception— ALL have been associated, in rare instance, with serious adverse effects, including death.<sup>23,24</sup> However, like lindane, they are relatively safe when used as directed.

#### Misleading Claim:

The risks of using lindane lotion and lindane shampoo outweigh any potential benefits.

#### Facts:

Repeated and extensive reviews conducted by medical and scientific experts working with the FDA have consistently determined that lindane medications have benefits that outweigh risks when used properly, and that the vast majority of serious adverse events associated with lindane have been due to misuse.<sup>25</sup> (See [Lindane Regulatory History](#))

The FDA has recognized the need to keep lindane on the market as a second-line medication for patients with scabies and lice who have failed or cannot tolerate first-line therapies.<sup>25</sup> (See [Regulatory Viewpoints on Lindane](#))

Previously packaged in 16 oz. bottles, lindane lotion and shampoo are now limited to single-use, 2 oz. bottles. This has dramatically reduced the potential for misuse. (See [Lindane Product Advancements](#))

Updates to the lindane prescription label on risks and proper use and a patient-friendly medication guide that is required by law to be dispensed with each prescription further promote the safety of lindane.<sup>25</sup>

#### Misleading Claim:

Lindane medications cause cancer in humans.

#### Facts:

To date, there has been no established link between the use of lindane medications and cancer in humans, despite over 50 years of clinical use for scabies and lice.<sup>26-28</sup> (See [Lindane and Cancer Risk](#))

An epidemiologic review of a 140,000-patient database published in 1997 concluded: "There is still no persuasive evidence from studies of humans that lindane, as ordinarily used clinically, is carcinogenic in humans."<sup>26</sup>

In 2001, the EPA downgraded the cancer-causing potential of lindane to the same low-level rating as other first-line scabies and lice medications, concluding that "[q]uantification of human cancer risk is not required."<sup>28</sup>

In 2004, the World Health Organization and the Food and Agricultural Organization of the United Nations Joint Meeting on Pesticide Residues (JMPR) similarly concluded that "In the absence of genotoxicity [ability to damage DNA] and on the basis of the weight of the evidence from the studies of carcinogenicity, JMPR has concluded that lindane is not likely to pose a carcinogenic risk to humans."<sup>29</sup>

### Misleading Claim:

Lindane medications are an important cause of childhood brain cancer.

### Facts:

This statement is scientifically unsupported as determined by the FDA.<sup>20</sup> The study that formed the basis of this claim was highly flawed and did not evaluate the use of lindane medications specifically but rather a variety of insecticidal chemicals used in the home, including no pest strips and flea collars.<sup>30</sup> (See Davis JR, et al. 1993)

In fact, the study by Davis JR, et al. triggered a special review by the FDA's Dermatologic Advisory Committee the same year it was published, which concluded that "[T]here were several flaws in the data presented in the article and that there was an unlikely association [between use of lindane medications and childhood brain cancer] based on the data. The committee voted that lindane was safe when properly used, and that it should remain on the market."<sup>20</sup> As such, no change in the lindane prescription labeling was considered necessary.

Even the authors of the study stated that "Given the large number of comparisons in the study, several of the significant findings may be due to chance alone."<sup>30</sup> Again, Lindane medications have not been shown to cause cancer in humans in the 50+ years they have been used in healthcare as discussed above. (See Lindane and Cancer Risk)

### Misleading Claim:

Banning lindane in the U.S. for medical purposes will eliminate the use of lindane for the treatment of scabies and lice and protect patients from associated risks.

### Facts:

The availability of U.S.-manufactured lindane eliminates the need for patients with no other treatment options to turn to Canadian suppliers, through websites or alternative channels, for less-regulated lindane products. (See Lindane Product Advancements)

In Canada, lindane is available without a prescription in bottle sizes as large as 17 oz.—enough lindane for 8 or more treatments—and is not accompanied by a patient medication guide on important safety warnings and proper use.

The FDA has recently warned Canadian drug importers about consistent misrepresentation of the safety of foreign drug products and failure to include

important patient safety information.

### Misleading Claim:

Lindane is no longer registered by the EPA for veterinary use in the U.S. due to its potential to cause cancer and birth defects.

### Facts:

In September of 1985, the EPA issued a Registration Standard for Lindane, requiring registrants of agricultural and veterinary lindane products to submit new data to support existing registrations and address human exposure levels (note that animal safety was not a factor as has been purported by special interest groups). Given the expense of conducting such studies relative to the profitability of such uses, no such studies were undertaken and all registered veterinary uses of lindane were voluntarily cancelled by registrants between 1998 and 2001.<sup>32</sup>

Moreover, the use of lindane veterinary products on large farm animals and domestic pets (often in the form of dips and sprays) resulted in much greater levels of human exposure compared with the FDA-approved medications, which are applied to skin or hair in small amount and in low concentration, typically as one-time treatments. Further, the human health risks associated with the use of lindane veterinary products were not balanced by any human health benefits, as is the case with lindane medications.

Indeed, the FDA has consistently maintained that lindane medications provide important health benefits that outweigh potential risks when used as directed.<sup>20</sup> The EPA has similarly concluded that lindane medications do not pose significant risks to the public or the environment when used as currently labeled.<sup>27,33</sup> (See false cancer claims above)

### Misleading Claim:

A single treatment of lindane shampoo or lotion for head lice or scabies pollutes 6 million gallons of water.

### Facts:

In the real world, lindane rinsed down the drain does not go directly into public drinking water reservoirs, but into the sewage system instead. (See [Lindane and Drinking Water Contamination](#))

If the above claim were true, large-scale water contamination testing programs would have detected lindane at unacceptably high levels in public drinking water supplies. However, this is not the case.

In 2003, the EPA reported test results of water samples collected from over 16,000 municipal water systems and found that none contained unsafe levels of lindane.<sup>34</sup> U.S. Geologic Survey teams noted the same results in their testing of streams across 30 states, which was conducted a few years earlier (1999 and 2000) when lindane medications were more commonly prescribed. It is also important to note that none of the testing distinguished between lindane from medical and agricultural sources, the latter of which has accounted for more than 99% of all lindane use in the U.S.<sup>32</sup>

Moreover, an unrealistic worst-case scenario analysis by Dr. Shayne Gad— an expert toxicologist— using 2004 Albany, NY water supply data, showed that even if 100% of lindane medications prescribed in that area (assuming proportional use across the state) had been poured directly into drinking water reservoirs, lindane levels would still be well below those considered unsafe by the EPA.<sup>34-37</sup>

Similarly, the EPA concluded as part of its reregistration eligibility decision for agricultural lindane that “[T]he Agency does not have risk concerns for concentrations of lindane in surface water used as a source of drinking water from consumer use for both lice and scabies treatments.”<sup>27</sup> (See [2006 EPA RED for Agricultural Lindane](#))

#### Misleading Claim:

Lindane is the 32nd most toxic chemical in the environment.

#### Facts:

This claim is based on a list of potentially hazardous substances put together by the CDC's Agency for Toxic Substances and Disease Registry (ASTDR). Chlorine and ammonia are also included on this list.<sup>38</sup>

It is important to point out that this list is not a list of most hazardous substances, but rather a list of substances that are monitored by this group based on a number of different factors. Highlighted in bold in the ASTDR report is the following statement: “It should be noted that this priority list is not a list of ‘most toxic’ substances, but rather a prioritization of substances based on a combination of their frequency, toxicity, and potential for human exposure at NPL sites.” (NPL, or National Priority List, sites are industrial facilities that generate chemical waste)<sup>38</sup>

Additionally, more than 99% of all lindane sold in the U.S. has been for agricultural purposes, not healthcare.<sup>32</sup> (See [Healthcare vs. Agricultural Uses of Lindane](#)) Further, the EPA concluded as part of its reregistration eligibility decision for agricultural lindane that lindane medications do not pose a significant risk to the environment.<sup>27</sup> (See [Points of View on Lindane: EPA](#))

#### Misleading Claim:

Lindane persists indefinitely in streams, sewers, and in the soil.

#### Facts:

According to the CDC's Agency for Toxic Substances and Disease Registry (ATSDR), lindane is broken down into less harmful substances by algae, fungi, and bacteria in soil, sediments, and water.<sup>39</sup>

Lindane is classified chemically as a hexachlorocyclohexane (HCH). There are many different forms (or isomers) of HCH. Lindane is the gamma form of HCH and is the only isomer with insecticidal activity.<sup>32</sup> (See [What is Lindane?](#))

Alpha-HCH and beta-HCH are notably the more toxic isomers and are the dominant forms found in the environment as well as in animal and human tissues and fluids.<sup>32,40</sup> (See [Healthcare vs. Agricultural Uses of Lindane](#))

Please See [Important Safety Information of Lindane](#)



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The risks of using lindane lotion and lindane shampoo outweigh any potential benefits.

#### Facts:

Repeated and extensive reviews conducted by medical and scientific experts working with the FDA have consistently determined that lindane medications have benefits that outweigh risks when used properly, and that the vast majority of serious adverse events associated with lindane have been due to misuse.<sup>25</sup> (See [Lindane Regulatory History](#))

The FDA has recognized the need to keep lindane on the market as a second-line medication for patients with scabies and lice who have failed or cannot tolerate first-line therapies.<sup>25</sup> (See [Regulatory Viewpoints on Lindane](#))

Previously packaged in 16 oz. bottles, lindane lotion and shampoo are now limited to single-use, 2 oz. bottles. This has dramatically reduced the potential for misuse. (See [Lindane Product Advancements](#))

Updates to the lindane prescription label on risks and proper use and a patient-friendly medication guide that is required by law to be dispensed with each prescription further promote the safety of lindane.<sup>25</sup>

#### Misleading Claim:

Lindane medications cause cancer in humans.

#### Facts:

To date, there has been no established link between the use of lindane medications and cancer in humans, despite over 50 years of clinical use for scabies and lice.<sup>26-28</sup> (See [Lindane and Cancer Risk](#))

An epidemiologic review of a 140,000-patient database published in 1997 concluded: "There is still no persuasive evidence from studies of humans that lindane, as ordinarily used clinically, is carcinogenic in humans."<sup>26</sup>

In 2001, the EPA downgraded the cancer-causing potential of lindane to the same low-level rating as other first-line scabies and lice medications, concluding that "[q]uantification of human cancer risk is not required."<sup>28</sup>

In 2004, the World Health Organization and the Food and Agricultural Organization of the United Nations Joint Meeting on Pesticide Residues (JMPR) similarly concluded that "In the absence of genotoxicity [ability to damage DNA] and on the basis of the weight of the evidence from the studies of carcinogenicity, JMPR has concluded that lindane is not likely to pose a carcinogenic risk to humans."<sup>29</sup>

### Misleading Claim:

Lindane medications are an important cause of childhood brain cancer.

### Facts:

This statement is scientifically unsupported as determined by the FDA.<sup>20</sup> The study that formed the basis of this claim was highly flawed and did not evaluate the use of lindane medications specifically but rather a variety of insecticidal chemicals used in the home, including no pest strips and flea collars.<sup>30</sup> (See Davis JR, et al. 1993)

In fact, the study by Davis JR, et al. triggered a special review by the FDA's Dermatologic Advisory Committee the same year it was published, which concluded that "[T]here were several flaws in the data presented in the article and that there was an unlikely association [between use of lindane medications and childhood brain cancer] based on the data. The committee voted that lindane was safe when properly used, and that it should remain on the market."<sup>20</sup> As such, no change in the lindane prescription labeling was considered necessary.

Even the authors of the study stated that "Given the large number of comparisons in the study, several of the significant findings may be due to chance alone."<sup>30</sup> Again, Lindane medications have not been shown to cause cancer in humans in the 50+ years they have been used in healthcare as discussed above. (See Lindane and Cancer Risk)

### Misleading Claim:

Banning lindane in the U.S. for medical purposes will eliminate the use of lindane for the treatment of scabies and lice and protect patients from associated risks.

### Facts:

The availability of U.S.-manufactured lindane eliminates the need for patients with no other treatment options to turn to Canadian suppliers, through websites or alternative channels, for less-regulated lindane products. (See Lindane Product Advancements)

In Canada, lindane is available without a prescription in bottle sizes as large as 17 oz.—enough lindane for 8 or more treatments—and is not accompanied by a patient medication guide on important safety warnings and proper use.

The FDA has recently warned Canadian drug importers about consistent misrepresentation of the safety of foreign drug products and failure to include

important patient safety information.

#### Misleading Claim:

Lindane is no longer registered by the EPA for veterinary use in the U.S. due to its potential to cause cancer and birth defects.

#### Facts:

In September of 1985, the EPA issued a Registration Standard for Lindane, requiring registrants of agricultural and veterinary lindane products to submit new data to support existing registrations and address human exposure levels (note that animal safety was not a factor as has been purported by special interest groups). Given the expense of conducting such studies relative to the profitability of such uses, no such studies were undertaken and all registered veterinary uses of lindane were voluntarily cancelled by registrants between 1998 and 2001.<sup>32</sup>

Moreover, the use of lindane veterinary products on large farm animals and domestic pets (often in the form of dips and sprays) resulted in much greater levels of human exposure compared with the FDA-approved medications, which are applied to skin or hair in small amount and in low concentration, typically as one-time treatments.

Further, the human health risks associated with the use of lindane veterinary products were not balanced by any human health benefits, as is the case with lindane medications.

Indeed, the FDA has consistently maintained that lindane medications provide important health benefits that outweigh potential risks when used as directed.<sup>20</sup> The EPA has similarly concluded that lindane medications do not pose significant risks to the public or the environment when used as currently labeled.<sup>27,33</sup> (See false cancer claims above)

#### Misleading Claim:

A single treatment of lindane shampoo or lotion for head lice or scabies pollutes 6 million gallons of water.

#### Facts:

In the real world, lindane rinsed down the drain does not go directly into public drinking water reservoirs, but into the sewage system instead. (See Lindane and Drinking Water Contamination)

If the above claim were true, large-scale water contamination testing programs would have detected lindane at unacceptably high levels in public drinking water supplies. However, this is not the case.

In 2003, the EPA reported test results of water samples collected from over 16,000 municipal water systems and found that none contained unsafe levels of lindane.<sup>34</sup> U.S. Geologic Survey teams noted the same results in their testing of streams across 30 states, which was conducted a few years earlier (1999 and 2000) when lindane medications were more commonly prescribed. It is also important to note that none of the testing distinguished between lindane from medical and agricultural sources, the latter of which has accounted for more than 99% of all lindane use in the U.S.<sup>32</sup>

Moreover, an unrealistic worst-case scenario analysis by Dr. Shayne Gad— an expert toxicologist— using 2004 Albany, NY water supply data, showed that even if 100% of lindane medications prescribed in that area (assuming proportional use across the state) had been poured directly into drinking water reservoirs, lindane levels would still be well below those considered unsafe by the EPA.<sup>34-37</sup>

Similarly, the EPA concluded as part of its reregistration eligibility decision for agricultural lindane that “[T]he Agency does not have risk concerns for concentrations of lindane in surface water used as a source of drinking water from consumer use for both lice and scabies treatments.”<sup>27</sup> (See 2006 EPA RED for Agricultural Lindane)

#### Misleading Claim:

Lindane is the 32nd most toxic chemical in the environment.

#### Facts:

This claim is based on a list of potentially hazardous substances put together by the CDC's Agency for Toxic Substances and Disease Registry (ASTDR). Chlorine and ammonia are also included on this list.<sup>38</sup>

It is important to point out that this list is not a list of most hazardous substances, but rather a list of substances that are monitored by this group based on a number of different factors. Highlighted in bold in the ASTDR report is the following statement: “It should be noted that this priority list is not a list of ‘most toxic’ substances, but rather a prioritization of substances based on a combination of their frequency, toxicity, and potential for human exposure at NPL sites.” (NPL, or National Priority List, sites are industrial facilities that generate chemical waste)<sup>38</sup>

Additionally, more than 99% of all lindane sold in the U.S. has been for agricultural purposes, not healthcare.<sup>32</sup> (See Healthcare vs. Agricultural Uses of Lindane) Further, the EPA concluded as part of its reregistration eligibility decision for agricultural lindane that lindane medications do not pose a significant risk to the environment.<sup>27</sup> (See Points of View on Lindane: EPA)

#### Misleading Claim:

Lindane persists indefinitely in streams, sewers, and in the soil.

#### Facts:

According to the CDC's Agency for Toxic Substances and Disease Registry (ATSDR), lindane is broken down into less harmful substances by algae, fungi, and bacteria in soil, sediments, and water.<sup>39</sup>

Lindane is classified chemically as a hexachlorocyclohexane (HCH). There are many different forms (or isomers) of HCH. Lindane is the gamma form of HCH and is the only isomer with insecticidal activity.<sup>32</sup> (See What is Lindane?)

Alpha-HCH and beta-HCH are notably the more toxic isomers and are the dominant forms found in the environment as well as in animal and human tissues and fluids.<sup>32,40</sup> (See Healthcare vs. Agricultural Uses of Lindane)

Please See Important Safety Information of Lindane



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